Paper No. 38

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PHILLIP DAN COOK, MUTHIAH MANOHARAN, and CHARLES J. GUINOSSO

Appeal No. 2001-2643
Application No. 08/117,363

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-29, all of the claims remaining. Claim 1 is representative and reads as follows:

1. A compound comprising a plurality of linked nucleosides, wherein:

each nucleoside includes a pentofuranosyl sugar portion and a base portion; and

at least one of said nucleosides bears at a 2'-O- position, a 3'-O- position, or a 5'-O- position a terminal substituent having formula:

$$-R_A-N(R_{1a})(R_{1b})$$

where:

R_A is alkyl having from 1 to about 10 carbon atoms or $(CH_2\text{-}CH_2\text{-}Q)_x$;

R_{1a} and R_{1b}, independently, are H, R_2, or an amine protecting group or have formula $C(X)\text{-}R_2$, $C(X)\text{-}R_A\text{-}R_2$, $C(X)\text{-}Q\text{-}R_A\text{-}R_2$, $C(X)\text{-}Q\text{-}R_2$; and

R_2 is a folate, a steroid molecule, a reporter molecule, a lipophilic molecule, a reporter enzyme, a peptide, a protein, or has formula $\text{-}Q\text{-}(CH_2CH_2\text{-}Q\text{-})_X\text{-}R_3$;

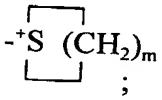
X is O or S;

each Q is independently, is NH, O, or S;

x is about 1 to about 50;

R_3 is H, R_A, C(O)OH, $C(O)OR_A$, $C(O)R_4$, $R_A\text{-}N_3$, or $R_A\text{-}\ NH_2$;

R_4 is Cl, Br, I, $SO_2\ R_5$ or has structure:



;

m is 2 to 7; and

R_5 alkyl having 1 to about 10 carbon atoms.

The examiner relies on the following references:

Urdea et al. (Urdea)		4,910,300	Mar. 20, 1990
Carrico		4,743,535	May. 10, 1988
Matteucci	WO	92/05186	Apr. 02, 1992
Latham	WO	91/14696	Oct. 03, 1991

Claims 1-4, 6-18, and 20-29 stand rejected under 35 U.S.C. § 103 as obvious in view of Urdea, Carrico, Matteucci, and Latham.

Claims 5 and 19 stand rejected under 35 U.S.C. § 103 as obvious in view of Urdea, Carrico, Matteucci, Latham, and "applicant[']s admissions."

We reverse.

Discussion

The claims are directed to nucleosides, and compounds comprising them, which are modified to have a terminal amine substituent in the 2'-O-, 3'-O-, or 5'-O-position, where the substituent is defined by a chemical formula. See, e.g., claim 1. The claimed products can also comprise moieties such as "a steroid molecule, a reporter molecule, a lipophilic molecule, a reporter enzyme, a peptide, [or] a protein." Claim 1. The specification discloses that the claimed products are useful in, among other things, antisense methodologies. See pages 7 and 9.

The examiner rejected all of the claims as obvious in view of Urdea, Carrico, Matteucci, and Latham, either alone or in combination with "applicants[']admissions."[1] The examiner reasoned as follows:

> Urdea et al. teaches a 5'-O-position having an R1 substituent (see Urdea bottom of col[.] 10). Matteucci discloses the claimed "O-C-N" chain (see Matteucci p. 16 lines 30-35) as well as numerous other internucleotide linkages (see Matteucci page 13, line 2 to page 20 line 30, for example).
>
> The claims differ from Matteucci in the recitation of terminal linkages. Latham teaches that internucleotide linkages and terminal linkages are art recognized alternatives (see for example Latham page 18, lines 3-17). Latham also teaches the attachment of linkages at the 2' position of the sugar.
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the prior art teachings [of] nucleotide linkages because, lacking a showing of criticality, or other secondary consideration, the claimed alkyl chain is considered one of several alternative linkages, any one of which the art skilled [worker] would reasonably expect to function in the

[1] The examiner relied on Appellants' "admissions" only to meet the specific limitation of claims 5 and 19. The basic rationale of both rejections was the same. See the Examiner's Answer, pages 4-5.

> claimed invention. Furthermore, Ca[r]rico discloses . . . the non-critical nature of the various 5' substitutions used for tethering labels to a nucleic acid. Ca[r]rico discloses, for example at col. 7, lines 15 and 22, that R1 is a "bond or a chain."

Examiner's Answer, pages 3-4.

Appellants argue that the "Examiner has not identified any reason" why a person of ordinary skill would have been motivated to modify the cited references as proposed. See the Appeal Brief, page 4. Appellants argue that both Latham and Matteucci propose one group of moieties as being appropriate for terminal linkage to the 2' position and an entirely different group as appropriate for internucleotide (3' or 5') linkages. Appeal Brief, page 5. Thus, Appellants argue, a person of ordinary skill in the art

> would not have been motivated to modify the teachings of the prior art in the manner proposed by the Examiner. There is simply no reason why a person of ordinary skill would have been motivated to take one of the non-terminal, 3'-5' internucleoside linkages disclosed by the Matteucci reference (such a linkage being covalently bound at both of its ends) and then attach it in a terminal manner at the 2'-position (so as to be covalently bound at only one end).

Id.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). "Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested

to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have had a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1443 (Fed. Cir. 1991) (citation omitted).

In this case, we agree with Appellants that the examiner has not adequately explained why a person of ordinary skill in the art would have been led to combine the teachings of the cited references. Matteucci and Latham are the most relevant to the examiner's rejection. As the examiner stated, Matteucci discloses oligonucleotides having linking groups that meet the limitations of the instant claims, but discloses those groups as internucleotide linkers, not as terminal substituents. The examiner relies on Latham for the suggestion to attach Matteucci's groups as terminal substituents, on the basis that "Latham teaches that internucleotide linkages and terminal linkages are art recognized alternatives."

The examiner's position is not supported by the evidence. Matteucci teaches that the disclosed linking groups have the property of being resistant to nuclease degradation and therefore render the oligonucleotide stable in vivo. See page 4, lines 28-33. Latham, on the other hand, teaches oligonucleotides linked, via a linking group, to a "transport agent," where the linkage is designed to

be cleaved under intracellular conditions, so as to release the oligonucleotide from the transport agent. See, e.g., page 10, lines 19-35.

The examiner has not adequately shown that the prior art would have suggested combining these teachings of different linking groups, having different properties, and located in different locations on the oligonucleotides, in the manner required to produce the invention of instant claim 16. "Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight." In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted). The rejections under 35 U.S.C. § 103 are reversed.

Other Issues

1. Claims 16-29

The examiner's rejections focus on the oligonucleotides of claim 1. Claim 16 is directed to a nucleoside having the same amine substituent as recited in claim 1 at the 2'-O-, 3'-O-, or 5'-O-position. Since the claim is directed to the unlinked nucleoside, an amine substituent at any of these positions would necessarily be a terminal substituent. According to the formula recited in claim 16, the amine substituent can be a C1 alkyl group linked to a nitrogen having R_{1a} and R_{1b} substituents, both of which can be hydrogen. Thus, the amine substituent can be $-CH_2NH_2$.

Matteucci discloses synthetic methods that utilize modified nucleosides that appear to meet the limitations of claim 16. See, e.g., compound 5 in Figure

1A. Matteucci describes this compound as "a 5-deoxy, 5'-amino, 3'-protected nucleoside, which can be selected from a range of known compounds." Page 28, lines 8-10.

The instant application claims priority through a series of continuations-in-part, to application 07/566,977 (filed August 13, 1990). Matteucci was published April 2, 1992. In disputing the examiner's rejections, however, Appellants have not argued that Matteucci is not prior art with respect to the instant claims. Thus, Matteucci seems to indicate that the compound of at least claim 16 was known in the art prior to its effective filing date. Upon return of this application, the examiner should consider whether Matteucci's disclosure anticipates or renders obvious claim 16 or the claims dependent thereon.

2. Inventorship

A petition was filed under 37 CFR 1.48(a) to correct the inventorship of the instant application by adding Charles J. Guinosso to the named inventors. See Paper No. 29, filed January 7, 1998. The examiner indicated that the petition had been granted and that "[t]he new inventor, Charles J. Guinosso, will be added to the file label immediately following the mailing of [Paper No. 31]." See Paper No. 31, mailed April 2, 1998.

The inventorship has not yet been changed on the face of the file or in the USPTO's computer database. Upon return of this application, the examiner should ensure that its inventorship accurately reflects the change requested in the granted petition.

Summary

The examiner has not adequately shown that the cited references would have suggested the claimed oligonucleotides to a person of ordinary skill in the art. Therefore, the rejection under 35 U.S.C. § 103 is reversed.

REVERSED

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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